P. ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing: 21 October 1999 (21.10.99)	
International application No.: PCT/GB98/03071	Applicant's or agent's file reference: PBA/D088026WO
International filing date: 14 October 1998 (14.10.98)	Priority date: 16 October 1997 (16.10.97)
Applicant: CLARKE, David, John et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International preliminary Examining Authority on:

22 March 1999 (22.03.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: J. Zahra

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

ATKINSON, Peter, Birch
Marks & Clerk
Sussex House
83-85 Mosley Street
Manchester M2 3LG
ROYAUME-UNI

Date of mailing (day/month/year)
20 April 2000 (20.04.00)

Applicant's or agent's file reference
PBA/D088026WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB98/03071

International filing date (day/month/year)
14 October 1998 (14.10.98)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
AOJULA, Harmesh, Singh Old Dutch Barn Doctor Lane Scouthead, Saddleworth Oldham OL4 4AD United Kingdom	GB	GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
Additional applicant/inventor for the purposes of the US.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Aino Metcalfe
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREAT

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
PBA/D088026WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 98/ 03071	14/10/1998	16/10/1997
Applicant		
THE VICTORIA UNIVERSITY OF MANCHESTER et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [X] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [X] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title,**
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. 3
   - [X] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

Inter. [redacted] Application No
PCT [redacted] 98/03071

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/127 G01N33/569 G01N33/58

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 98 16240 A (THE LIPOSOME COMPANY, INC.) 23 April 1998 see the whole document	1-4,11, 17,19, 22,23, 25,27, 28,30,31
A	WO 93 25225 A (UNIVERSITY OF MASSACHUSETTS MEDICAL CENTER) 23 December 1993 see the whole document	1-31
A	US 4 900 556 A (M. A. WHEATLEY ET AL.) 13 February 1990 see the whole document	1-31
A	EP 0 393 707 A (OTSUKA PHARMACEUTICAL CO., LTD.) 24 October 1990 see abstract	1-31

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 January 1999	01/02/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Griffith, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interr[redacted] Application No
PCT/GB 98/03071

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 885 172 A (M. B. BALLY ET AL.) 5 December 1989 see the whole document ---	1-31
A	WO 96 40060 A (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 19 December 1996 see abstract ---	1-31
A	US 5 525 232 A (J. A. VEIRO ET AL.) 11 June 1996 -----	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/[illegible] 98/03071

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9816240 A	23-04-1998	AU 4820797 A	11-05-1998
WO 9325225 A	23-12-1993	AU 4633893 A	04-01-1994
US 4900556 A	13-02-1990	NONE	
EP 393707 A	24-10-1990	DE 69013557 D	01-12-1994
		JP 3034920 A	14-02-1991
		KR 9404390 B	25-05-1994
US 4885172 A	05-12-1989	US 4880635 A	14-11-1989
		CA 1297787 A	24-03-1992
		CA 1323569 A	26-10-1993
		CA 1323570 A	26-10-1993
		MX 9203291 A	01-08-1992
		MX 9203797 A	01-08-1992
		US 5059421 A	22-10-1991
		US 5047245 A	10-09-1991
		US 5171578 A	15-12-1992
		US 5399331 A	21-03-1995
		AT 149347 T	15-03-1997
		AT 149346 T	15-03-1997
		CA 1270197 A	12-06-1990
		CA 1270198 A	12-06-1990
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		CA 1329548 A	17-05-1994
		DE 3587639 D	02-12-1993
		DE 3587639 T	24-03-1994
		DE 3587640 D	02-12-1993
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		DE 3588146 D	10-04-1997
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		EP 0562641 A	29-09-1993
		EP 0561424 A	22-09-1993
		IE 68686 B	10-07-1996
		JP 9020652 A	21-01-1997
		JP 2574999 B	22-01-1997
		JP 7145041 A	06-06-1995
		JP 2572553 B	16-01-1997
		JP 7165560 A	27-06-1995
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		JP 7112968 B	06-12-1995
		JP 62500101 T	16-01-1987
		JP 8018973 B	28-02-1996
		JP 62500102 T	16-01-1987
		PT 80926 B	30-09-1987
		US 5578320 A	26-11-1996

INTERNATIONAL SEARCH REPORT

[redacted] on patent family members

Inte[redacted]al Application No
PCT/GB 98/03071

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4885172 A		US 5409704 A	25-04-1995
		WO 8601102 A	27-02-1986
WO 9640060 A	19-12-1996	US 5643599 A	01-07-1997
		AU 5928696 A	30-12-1996
		CA 2223788 A	19-12-1996
		EP 0831778 A	01-04-1998
US 5525232 A	11-06-1996	NONE	

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PBA/D088026PWO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB98/03071	14/10/1998	16/10/1997
International Patent Classification (IPC) or national classification and IPC		
G01N33/569		
Applicant		
THE VICTORIA UNIVERSITY OF MANCHESTER et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22/03/1999	20.01.00
Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hinchliffe, P Telephone No. +49 89 2399 8431

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB98/03071

I. Basis of th r port

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-46 as originally filed

Claims, No.:

1-41 as received on 12/11/1999 with letter of 05/11/1999

Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they hav been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-41
	No:	Claims
Inventive step (IS)	Yes:	Claims 1-41
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-16,23-41
	No:	Claims 17-22

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

SECTION V

i) The priority documents of the present application were not available at the time that this report was written. Consequently the document cited as P'X' in the I.S.R. may become relevant to the question of novelty of some or all of the claims at a later stage of the procedure.

1. The claims (1-41) fulfill the requirements of Articles 33(2) and 33(3) PCT because they include the feature that the lipid vesicles contain a cytolytic peptide that controls the liposomes permeability in response to a metabolic signal. Such a feature provides novelty over the closest prior art D6 (as cited in the ISR) which discloses liposomes in which the permeability is controlled by a pH dependent lipid rather than a permeability inducing cytolytic peptide (as currently claimed). Furthermore the use of a modulator of permeability peptide which responds to a metabolic signal from the targeted cell is not shown in any of the prior art documents cited in the ISR. Consequently the subject matter of the claims also involves an inventive step.

2. Claims 17-22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D6 and D7 are not mentioned in the description, nor are these documents identified therein.

SECTION VIII

1. The only subject matter supported by the three examples is the detection/destruction of bacteria using a modified liposome/erythrocyte that is pH sensitive (thanks to a pH sensitive lipid). It is emphasised that the

method is only shown to work with bacterial cells. No actual results *in vivo* or with other cell types (e.g. eukaryotic) are shown and consequently these aspects of the invention fail to find support in the application, contrary to the requirements of Art.6 PCT.

In more detail:

i). The claimed methods: arguments along the lines of " the common application of general knowledge" can not accepted when a claim is directed towards a highly complicated issue such as treatment of cancer. An *in vitro* lysis of a bacterial cell (either in the presence or absence of erythrocytes (ex. 3)) cannot be extrapolated to an *in vivo* system. The common general knowledge of a skilled person is more likely to be pessimistic about the application of such methods for *in vivo* treatment of disease. Consequently the claimed methods of treatment are not supported contrary to the requirements of Art.6 PCT.

ii). Cytolytic peptides that respond to a predetermined metabolic signal: Insofar as the skilled person would know that the GALA cytolytic peptide exemplified is related to HELP, KALA and LAGA, the references to these cytolytic peptides, in claims 7,8,26,27, are fully supported by the description. However the generic reference to cytolytic peptides is not fully supported because the skilled person would first of all have to detect a metabolic signal produced by the cell to be targeted and then find a peptide which would increase the permeability of a liposome in response to this signal. Such a task is considered to be beyond what could be expected of the skilled person.

In addition the references to Amphotericin, Alamethicin..... (see claims 9,28) cannot be regarded as being fully supported by the description either because they are not shown to react to a metabolic signal produced by a target cell by increasing their permeabilisation of a liposome.

iii). Types of cell treated: The only cells targeted in the examples are bacterial cells in *ex vivo* (i.e. outside of a living organism) food and water samples. Such cells are quite different to, for example, cancer cells. The skilled person would, in the opinion of the examiner, have an undue burden placed

upon her/him in order to adapt the particles to identify/destroy other cell types. Furthermore the conditions in which the cells are found are also quite different; bacterial contamination of food or water provides a totally different environment to that of, for example, a cell found making up an organ. Consequently all of the types of cell treated are not supported contrary to the requirements of Art.6 PCT.

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 9/127, G01N 33/569, 33/58

A1

(11) International Publication Number: WO 99/20252

(43) International Publication Date: 29 April 1999 (29.04.99)

(21) International Application Number: PCT/GB98/03071

(22) International Filing Date: 14 October 1998 (14.10.98)

(30) Priority Data:
9721901.8 16 October 1997 (16.10.97) GB

(71) Applicant *(for all designated States except US)*: THE VICTORIA UNIVERSITY OF MANCHESTER [GB/GB]; Oxford Road, Manchester M13 9PL (GB).

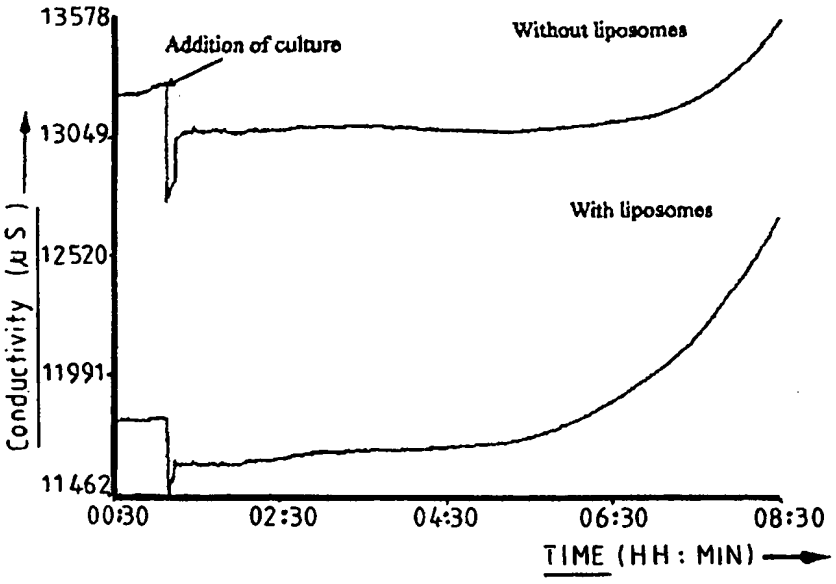
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: CLARKE, David, John [GB/GB]; 6 Fields Drive, Sandbach, Cheshire EW11 1YB (GB). HARRISON, Michael, Henry [GB/GB]; 12 South Marlow Street, Hadfield, Hyde SK14 8AL (GB).

(74) Agent: ATKINSON, Peter, Birch; Marks & Clerk, Sussex House, 83–85 Mosley Street, Manchester M2 3LG (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: PARTICLES



(57) Abstract

Lipid vesicle particles capable of being targeted to a cell type of interest, said particle incorporating a peptide which is responsive to a predetermined metabolic signal from the targeted cell so as to modulate the permeability of the particle, said particle further incorporating a species to be targeted to the cell which is activated on said modulation of permeability. The particles may be used in methods for detecting cells, methods of treating cells and also therapeutically.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia	**LR**	Liberia	**SG**	Singapore		

CLAIMS

1. A lipid vesicle particle capable of being targeted to a cell type of interest, said particle incorporating a peptide which is responsive to a predetermined metabolic signal from the targeted cell so as to modulate the permeability of the particle, said particle further incorporating a species to be targeted to the cell which is activated on said modulation of permeability.

2. The particle according to claim 1, wherein the particle has an outer lipid bilayer and the metabolic signal modulates the permeability of the lipid bilayer.

3. The particle according to claim 1 or claim 2 wherein the particle is a liposome.

4. The particle according to any preceding claim wherein the peptide is a cytolytic agent.

5. The particle according to claim 4 wherein the peptide is N. Myristic-GALA.

6. The particle according to any one of claims 1 - 3 wherein the peptide is one selected from the group consisting of Aerolysin, Amphotericin B, Aspergillus haemolysin, Alamethicin, A-23187 (Calcium ionophore), Apolipoproteins, ATP Translocase, Cereolysin, Colicins. Direct lytic factors from animal venoms, Diptheria toxin, Filipin, GALA, Gramicidin, Helical erythrocyte lysing peptide (HELP), Hemolysins, Ionomycin, KALA, LAGA, Listeriolysin, Melittin, Metridiolysin, Nigericin, Nystatin, P25, Phospholipases, Polyene Antibiotics, Polymixin B, Saponin, Staphytlococcus aureus toxins (α,ß,χ,δ), Streptolysin O, Streptolysin S, Synexin, Surfactin, Tubulin, Valinomycin and Vibriolsin.

7. The particle according to any preceding claim wherein the particle incorporates a species which amplifies the metabolic signal from the cell.

8. The particle according to claim 7, wherein the amplifying species is an enzyme.

9. The particle according to claim 8, wherein the enzyme is alkaline phosphatase, β-Galactosidase or asparaginase, or glucose oxidase.

10. The particle according to claim 7, wherein the amplifying species is a co-factor or substrate for an enzyme.

11. The particle according to any preceding claim wherein the particle comprises an antibody for targeting to an antigen on a cell.

12. The particle according to any preceding claim wherein the particle further comprises a binding moiety for binding to other particles.

13. A collection of particles according to any preceding claim wherein a portion of said particles have a first binding moiety and a further portion have a second binding moiety which is capable of binding with said first binding moiety whereby said particles are, or are capable of being, aggregated together.

14 A collection of particles according to claim 13 wherein the first binding moiety is avidin or a derivative thereof and the second binding moiety is biotin or a derivative thereof.

15 An aggregate comprising a collection of particles according to claim 13 or claim 14.

16. An aggregate comprising a plurality of lipid vesicle particles according to any one of claims 1 - 12 wherein a portion of said particles have a first binding moiety and a further portion have a second binding moiety capable of binding with said first binding moiety whereby said particles are aggregated together.

17. A method of detecting cells which are present or potentially present in a sample comprising treating the sample with particles capable of being targeted to a cell type of interest, said particles incorporating a species that is directly or indirectly detectable when activated in response to a predetermined metabolic signal from the targeted cell, and monitoring for directly or indirectly the species.

18. The method according to claim 15 wherein the particles are according to any one of claims 1 - 12 or an aggregate of particles according to claim 15 or claim 16.

19. The method according to claim 17 or claim 18 wherein the cells to be detected are pathogenic cells.

20. The method according to claim 19 for analysing foodstuff for the presence of pathogenic cells.

21. The method according to claim 19 for analysing water samples for the presence of pathogenic cells.

22. The method according to claim 19 for detecting the presence of pathogenic cells in the human or animal body.

23. A method of treating cells comprising treating a cell requiring treatment a particle which incorporates a species which modulates cell activity when activated in response to a predetermined metabolic signal from the cells

24. The method according to claim 23 wherein the particle is a particle according to any one of claims 1 - 12 or an aggregate of particles according to claim 15 or claim 16.

25. The method according to claim 23 or claim 24 for treatment of pathogenic cells.

26. The method according to claim 25, wherein the treatment is the removal of pathogenic cells from a water source.

27. The method according to any one of claims 17 - 26 wherein the cell is a bacterium.

28. A particle capable of being targeted to a cell that incorporates a therapeutically effective amount of a species which is activated in response to a predetermined metabolic signal from a cell, for use in the treatment of medical conditions.

29. The method according to claim 28 wherein the particle is a particle according to any one of claims 1 - 12 or an aggregate of particles according to claim 15 or claim 16.

30. The use of a particle according to claim 29 for the treatment of cancer.

31. The use of a particle according to claim 29 for the treatment of microbial infections.